cyanocobalamin or folic acid; during treatment with antimetabolic drugs or irradiation; in reactive change, as in haemolytic anaemias; in the course of acute infections, particularly hepatitis. The change has also been described in pigs made experimentally deficient in vitamin E. The giant erythroblasts in the bone marrow smear are usually accompanied by scanty macrocytes in an otherwise normochromic normocytic peripheral blood film.

This paper describes such changes in two dissimilar types of case: in refractory sideroblastic anaemia which in many cases should be regarded as a myeloproliferative disorder; and as a transient phenomenon in cases of acute infection, particularly in two patients with acute hepatitis and an antitoxoplasma dye test titre of 1 in 256. Only one previous instance of an association between hepatitis and polyploid erythroblasts has been reported. There is a case for regarding this change as one of the cardinal signs of morphological haematology, a sign of varied pathological significance, but probably due to a failure of cytoplasmic division, which may in turn be brought about by inadequate synthesis of the cell membrane.

LABORATORY ASPECTS OF PHENYLKETONURIA DETECTION AND TREATMENT

S. F. CAHALANE (*Children's Hospital, Dublin*) Mass screening of newborns by the Guthrie and other blood techniques lead to the detection of hyperphenylalaninaemia. The possible causes of this in the newborn may be condensed into six situations: classical phenylketonuria (PKU); mild or atypical PKU; transient tyrosinaemia; delayed maturation of the phenylalanine hydroxylase system; maternal PKU; and finally a number of rarer enzyme defects.

The choice of a screening method depends on such criteria as simplicity of specimen collection and transport; simplicity of test; sensitivity and specificity of test; applicability to all newborns and finally inexpensiveness of the programme.

The available techniques are based on microbial inhibition, paper chromatography, and automated fluorimetry. The microbial inhibition test of Guthrie seems at present to meet the criteria most comprehensively. Screening centres should be based on adequate catchment areas and should not be set up for small units.

The laboratory investigation of the presumptive positive test depends in the first place on the initial blood level and the age at testing. The commonest cause for an elevated test is transient tyrosinaemia, generally associated with prematurity and seldom showing test levels greater than 8 mg of phenylalanine.

Newborns with classical PKU tend to achieve levels of 30 mg or higher in a short time. The interpretation of intermediate levels is more difficult and may depend on some or all of the following methods: (1) repeat quantita-

tive serum phenylalanine and tyrosine; (2) testing for urinary phenylpyruvic acid and O-hydroxyphenylacetic acid; (3) sibling and maternal blood tests and history; (4) phenylalanine tolerance tests on parents and/or infant; (5) enzyme assay on liver biopsy.

All cases of classical PKU and possibly all doubtful cases should be placed on a restricted diet. The doubtful cases can be reevaluated at about 3 or 4 months of age. Treatment must be monitored by regular biochemical assay of blood phenylalanine for which a number of reliable techniques are available.

CHLOROQUINE-RESISTANT *P. FALCIPARUM* INFECTIONS

A. R. T. LUNDIE (*Singapore*) The evidence of chloroquine-resistant *P. falciparum* malaria in Vietnam and Thailand is well known and has recently been reviewed by Peters (1969). Montgomery and Eyles (1963), Sandosham (1967), and Kellett, Cowan, and Parry (1968) have described evidence of resistant strains in the north of west Malaysia. Singapore is a malaria-free area. Since 1966 the British Army Medical Services have been conducting an investigation into the incidence of drug-resistant malaria in Malaya. McKelvey, Lundie, Williams, Moore, and Worsely (1968) reported the first evidence of chloroquine-resistant strains of *P. falciparum* from further areas, including south Johore. Investigations continue in cooperation with the Walter Reed Army Institute of Research in Washington and the Institute of Medical Research in Kuala Lumpur.

Laboratory studies were complementary to careful management by medical and nursing staff of a reference hospital in a malaria-free area to ensure that the World Health Organization field trial (1965) was applied. In addition to the examination of thick and thin blood films, on the first seven, the 14th, and 28th days of illness, Haskins' (1958) test was carried out on urine daily on the first seven days. Urine was also tested for proguanil (Gage and Rose, 1946) on admission.

The extension of the area in which chloroquine-resistant *P. falciparum* malaria may be acquired emphasizes the need for adequate laboratory investigation of patients with pyrexia of unknown origin who have been in west Malaysia.

REFERENCES

- Gage, J. C., and Rose, F. L. (1946). *Amer. trop. Med. Parasit.*, **40**, 333.
- Haskins, W. T. (1958). *Amer. J. trop. Med. Hyg.*, **7**, 199.
- Kellett, R. J., Cowan, G. O., and Parry, E. S. (1968). *Lancet*, **946**.
- McKelvey, T. P. H., Lundie, A. R. T., Williams, E. D. H., Moore, H. S., and Worsely, D. E. (1968). *Brit. med. J.*, **4**, 704.
- Montgomery, R., and Eyles, D. E. (1963). *Trans. roy. Soc. trop. Med. Hyg.*, **57**, 409.
- Peters, W. (1969). *Ibid.*, **63**, 25.
- Sandosham, A. A. (1967). *Med. J. Malaya*, **22**, 145.
- World Health Organization (1965). *Wld Hlth Org. techn. Rep. Ser.*, no. 296, 36.